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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: L. E. Crane Examiner #: 65753 Date: 08/04/00
Art Unit: 1623 Phone Number 30 8-4639 Serial Number: 09/363,748
Mail Box and Bldg/Room Location: CM1; 7E-15 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: see copy of claims attached

Inventors (please provide full names): "

Earliest Priority Filing Date: "

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for a method of treating a human for "neurological disorders by administration of uridine or source of uridine, and "other compounds including CHOLINE or choline ester (30-33

Disorders are defined in claims 5, 9, 12, 13-17, 18, 19, 20-28

also

OTHER COMPOUNDS - see claims 30-31, 33, 34, 35,

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****

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Type of Search

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PTO-1590 (1-2000)

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FILE 'HCAOLD' ENTERED AT 17:23:42 ON 07 AUG 2000
L19 1 S L8
L20 632 S URIDIN?
L21 5 S L20 AND ?NEUR?
L22 6 S L20 AND ?NERV?
L23 11 S L21,L22
L24 0 S L20 AND (MEMORY OR PICK OR LEWY OR DEMENT? OR SENIL? OR SENES
L25 3 S L20 AND (BEHAV? OR EMOTI? OR STRESS? OR PANIC OR ANXIET? OR A

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FILE 'HCAOLD' ENTERED AT 17:28:41 ON 07 AUG 2000

FILE 'HCAOLD' ENTERED AT 17:28:47 ON 07 AUG 2000
L26 1 S L20 AND (ATAX? OR FRIEDREICH? OR DYSKINES? OR ?THROMBO?)
L27 15 S L20 AND (ISCHEM? OR ISCHAEM? OR HYPOX? OR CEREBR? OR BRAIN OR
L28 1 S L20 AND (SPINAL OR SPINE OR ANOX? OR MYASTHEN? OR POLIO OR PO

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=> d all hitstr l28

L28 ANSWER 1 OF 1 HCAOLD COPYRIGHT 2000 ACS
AN CA57:10485f CAOLD
TI pharmacology of .alpha.-amino acids
AU Kowa, Yoshio
TI studies on the disturbances caused by dehydrocholic acid on the process of elimination of Bromsulfalein
AU Benda, Nello; Gambelunghe, C.
TI **uridine**-5-triphosphate in therapy - (I) cure of neurogenic muscular atrophy, (II) cure of myopathia, myotonia, **myasthenia**, and of asthenic condition
AU Coirault, R.; Levy, J.; Michel-Ber, E.; Masbernard, A.; Fonchais, S. D. de la; Mazingant, F.

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 17:45:08 ON 07 AUG 2000

FILE COVERS 1967 - 7 Aug 2000 VOL 133 ISS 7
FILE LAST UPDATED: 6 Aug 2000 (20000806/ED)

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L48 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:161074 HCAPLUS
DN 132:203149
TI Compositions and methods using pyrimidine nucleotide precursors for treatment of mitochondrial diseases
IN Von Borstel, Reid W.
PA Pro-Neuron, Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N043-04
ICS A61K031-70
CC 1-10 (Pharmacology)
Section cross-reference(s): 33, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000011952	A1	20000309	WO 1999-US19725	19990831 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960219	A1	20000321	AU 1999-60219	19990831 <--
PRAI US 1998-144096	19980831 <--			
WO 1999-US19725	19990831			

AB Compds., compns., and methods are provided for treatment of disorders related to mitochondrial dysfunction. The methods comprise administering to a mammal a compn. contg. pyrimidine nucleotide precursors in amts. sufficient to treat symptoms resulting from mitochondrial respiratory chain deficiencies.
ST mitochondrial disease treatment pyrimidine nucleotide precursor;

respiratory chain mitochondrial deficiency pyrimidine nucleotide precursor therapeutic

IT **Nervous** system
(**Friedreich**'s **ataxia**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Nervous** system
(**Huntington**'s chorea; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Muscle, disease
(Kearns-Sayre syndrome; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Brain**, disease
(Leigh's disease; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Brain**, disease
(MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes); pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Muscle, disease
(MERRF (myoclonic epilepsy assocd. with ragged-red muscle fibers); pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Disease, animal
(NARP (**neurogenic** muscle weakness, **ataxia**, and retinitis pigmentosa); pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Brain**, disease
(Rett syndrome; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Nervous** system
(**ataxia**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Mental disorder**
(**attention** deficit hyperactivity **disorder**; pyrimidine nucleotide precursors for treatment of mitochondrial **diseases**)

IT **Mental disorder**
(autism; pyrimidine nucleotide precursors for treatment of mitochondrial **diseases**)

IT **Nervous** system
(autonomic, **neuropathy**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Heart, disease
(cardiomyopathy, dilating; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Cytoprotective agents
(cardioprotective; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Muscle
(cell; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Fatigue, biological
(chemotherapy-assocd.; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Menopause
(chemotherapy-induced; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Fatigue, biological
(chronic fatigue syndrome; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Eye, disease
(chronic progressive external ophthalmoplegia; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Brain**
(corpus striatum, striatal dopamine content; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **Neuron**
(death; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Nervous** system
(degeneration; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Neuromuscular** diseases
(degenerative; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Mutation
(deletion; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Appetite
(**depressed**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Development, mammalian postnatal
(developmental delay in cognitive, motor, language, executive function, or social skills; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Bladder
(diseases, **neurogenic** bladder dysfunction; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Mitochondria
(diseases; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Toxins
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(excitotoxins; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Liver, disease
(failure; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Drugs
(gastrointestinal, for **neurogenic** bowel dysfunction; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Eye, disease
(hereditary optic atrophy; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Acidosis
(lactic acidosis; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Chemotherapy
(menopause induced by and fatigue assocd. with; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Diagnosis
(mitochondrial disease; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Brain**, disease
(mitochondrial encephalomyopathy, mitochondrial **neurogastrointestinal**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Proteins, general, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mitochondrial respiratory chain nuclear-encoded protein components; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Respiration, animal
(mitochondrial; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Behavior**
(motor, developmental delay in cognitive, motor, language, executive function, or social skills; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Heart

(myocyte; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Muscular dystrophy**
(myotonic; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Intestine, disease
(**neurogenic** bowel dysfunction; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Cell death
(**neuron**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Cytoprotective agents
(**neuroprotectants**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Nerve**
(optic, optic **neuropathy**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Nerve**, disease
(peripheral **neuropathy**; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Mitosis
(post-mitotic cell death or functional decline; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Aging, animal
Anti-**Alzheimer**'s agents
Anticonvulsants
Antimigraine agents
Antiparkinsonian agents
Cell death
Cognition enhancers
Cytoprotective agents
Drug delivery systems
Muscular dystrophy
Mutation
Nervous system agents
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Pyrimidine nucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Mitochondrial DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Acidosis
(renal tubular; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Mitochondria
(respiration; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Antitumor agents
Cytotoxic agents
(respiratory chain dysfunction from; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Deafness
(sensorineural; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT **Behavior**
(social, developmental delay in cognitive, motor, language, executive function, or social skills; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
IT Disease, animal
(speech **disorder**, **developmental** delay in cognitive,

motor, language, executive function, or social skills; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Hepatitis
(steatohepatitis; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT Kidney, disease
(tubular acidosis; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 33069-62-4, Taxol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(**neuropathy** induced by; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 89-00-9, Quinolinic acid 504-88-1, 3-Nitropropionic acid 28289-54-5, MPTP
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 260360-01-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT **58-96-8D, Uridine**, acyl derivs. 65-46-3, Cytidine 65-46-3D, Cytidine, acyl derivs. 65-86-1, Orotic acid 65-86-1D, Orotic acid, esters 127-17-3, Pyruvic acid, biological studies 127-17-3D, Pyruvic acid, esters **987-78-0**, Cytidine **diphosphocholine** 1747-53-1, Ethyl orotate 4105-38-8, 2',3',5'-Tri-O-acetyluridine 260360-02-9 260360-03-0 260360-04-1 260360-05-2 260360-06-3 260360-07-4
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 51-61-6, Dopamine, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 9000-83-3, Complex V (Mitochondrial electron transport) 9001-16-5, Mitochondrial electron transport complex IV 9027-03-6, Mitochondrial electron transport complex III 9028-04-0, Mitochondrial electron transport complex I 9028-11-9, Mitochondrial electron transport complex II
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

IT 5704-66-5
RL: RCT (Reactant)
(reaction; pyrimidine nucleotide precursors for treatment of mitochondrial diseases)

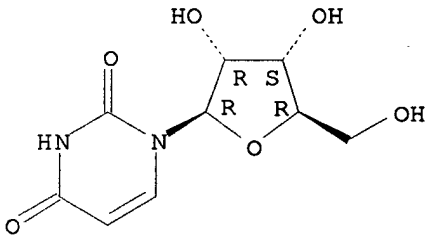
RE.CNT 5

RE

(1) Bodnar; Biochem J 1995, V305, P817 HCAPLUS
(2) Dykens, J; Journal of Neurochemistry 1994, V63, P584 HCAPLUS
(3) Keilbaugh; Molecular Pharmacology 1993, V44(4), P702 HCAPLUS
(4) Secades; Methods and Findings in Experimental and Clinical Pharmacology 1995, V17(Supplement 1), P1
(5) van Borstel; US 5470838 A 1995

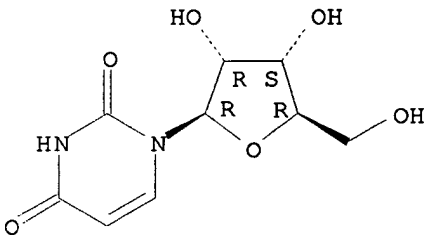
IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



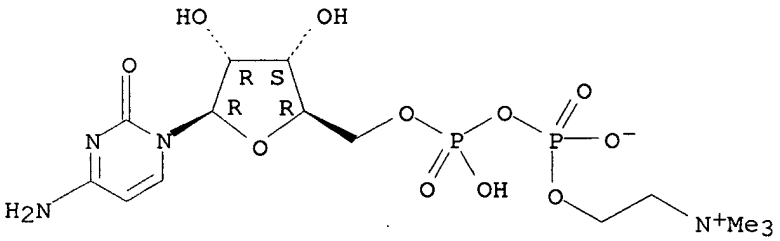
IT **58-96-8D, Uridine**, acyl derivs. **987-78-0**, Cytidine **diphosphocholine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pyrimidine nucleotide precursors for treatment of mitochondrial diseases)
RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 987-78-0 HCAPLUS
CN Cytidine 5'-(trihydrogen diphosphate), P'-[2-(trimethylammonio)ethyl] ester, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:98343 HCAPLUS
DN 132:132349
TI Methods using **uridine** or a **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human

neurological diseases
IN **Watkins, Carol; Wurtman, Richard J.**
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-55
ICS A61K031-70; A61K031-235; A61K031-515; A61K031-685
CC 1-11 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000006174	A1	20000210	WO 1999-US17235	19990730 <--

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1998-95002 19980731 <--
AB Methods of treating certain **neurol**. diseases using exogenous **uridine** or a **uridine** source alone as a precursor of endogenous cytidine, particularly in the human **brain**, are disclosed. Methods are also disclosed in which exogenous **uridine** or a **uridine** source is combined either with drugs increasing **uridine** availability or with compds. that serve as a source of **choline** in phospholipid synthesis.
ST **uridine** cytidine precursor **neurol** disease treatment; **choline** source **uridine neurol** disease treatment
IT AIDS (disease)
(AIDS **dementia** complex; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)
IT **Mental disorder**
(AIDS **dementia; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. **diseases**)
IT **Nervous** system
(**Friedreich**'s **ataxia; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)
IT **Nervous** system
(**Huntington**'s chorea; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)
IT **Mental disorder**
(**Pick**'s **disease; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. **diseases**)
IT **Mental disorder**
(affective, seasonal; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. **diseases**)
IT **Brain**
(aging, **memory** decline assocd. with; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)
IT **Mental activity**
(**alertness; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. **diseases**)
IT **Nervous** system
(**ataxia; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)
IT **Mental disorder**
(**attention** deficit **disorder; uridine** or

uridine source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT Aging, animal
(**brain, memory** decline assocd. with; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Hypoxia**, animal
(**cerebrovascular** disease from; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Brain**, disease
(**cerebrovascular, hypoxia**-caused; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Mental activity**
(concn. and **focus; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT HPLC
(cytidine-tyrosine sepn. in; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Mental disorder**
(**dementia; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Mental disorder**
(**depression, neurotic; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Mental disorder**
(diffuse **Lewy** body **disease; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Nervous** system
(disease; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Behavior**
Emotion
(disorder; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Mental disorder**
(**dyslexia; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Spinal** cord
(injury, **behavioral** or **neurol.** syndrome after **anoxia** or; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Mental disorder**
(**mania; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Mental disorder**
(**manic bipolar disorder; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol. diseases**)

IT **Anxiety**
(**panic; uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol.** diseases)

IT **Nervous** system

(peripheral, disease; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT Poliomyelitis
(post-**polio** syndrome; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **Brain**, disease
(stroke; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **Nervous** system
(tardive **dyskinesia**; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **Brain**, disease
(trauma, **behavioral** or **neurol**. syndrome after; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **Anti-ischemic** agents
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiolytics
Blood analysis
Cognition enhancers
Movement disorders
Muscular dystrophy
Myasthenia gravis
Nervous system agents
Neuromuscular diseases
Schizophrenia
Stress, animal
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **Fatty acids**, biological studies
Lecithins
Lysophosphatidylcholines
Sphingomyelins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT Biological transport
Kidney
(**uridine** renal transport competitors; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT 60-18-4, Tyrosine, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(cytidine-tyrosine sepn. in HPLC; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT 9030-22-2, **Uridine** phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT **58-96-8**, **Uridine**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine

levels in vivo and treating cytidine-dependent human **neurol**. diseases)

IT 65-46-3, Cytidine
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

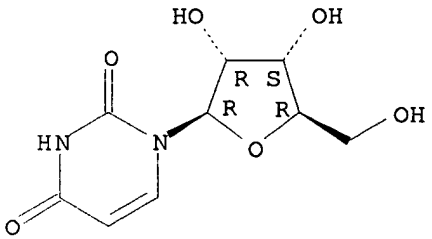
IT **54-03-5, Hexobendine 62-49-7, Choline 67-48-1, Choline** chloride **87-67-2, Choline** bitartrate **563-24-6, Glycerophosphatidylcholine 563-24-6D, Glycerophosphocholine**, acyl derivs. **987-78-0**, CDP-**choline 5909-45-5 5909-45-5D**, derivs. **5983-09-5**, 2',3'-**Dideoxyuridine 23464-76-8, Choline** stearate **26287-69-4**, L-**Uridine 35898-87-4, Dilazep 153547-98-9**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

RE.CNT 9
RE
(1) Bamat, M; WO 8903837 A
(2) Gallai, V; Ribista di Neuropsichiatria e Scienze Affini 1995
(3) Luca, D; US 4960759 A 1990
(4) Myers, C; Pharmacology biochemistry and Behavior 1995
(5) Page, T; Proc Natl Acad Sci U S A 1997 HCAPLUS
(6) Piazza, C; WO 9745127 A1 HCAPLUS
(7) Sommadossi; US 5567689 A 1996
(8) Von Borstel; US 5583117 A 1996
(9) Yamamoto, S; JP 09030976 A2 HCAPLUS

IT **58-96-8, Uridine**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

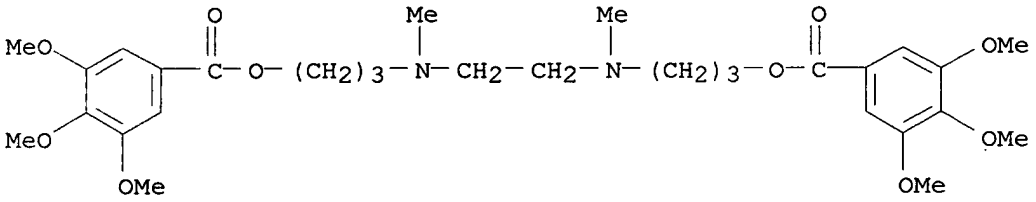
Absolute stereochemistry.



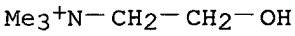
IT **54-03-5, Hexobendine 62-49-7, Choline 67-48-1, Choline** chloride **87-67-2, Choline** bitartrate **563-24-6, Glycerophosphatidylcholine 563-24-6D, Glycerophosphocholine**, acyl derivs. **987-78-0**, CDP-**choline 5909-45-5 5909-45-5D**, derivs. **5983-09-5**, 2',3'-**Dideoxyuridine 23464-76-8, Choline** stearate **26287-69-4**, L-**Uridine 35898-87-4, Dilazep 153547-98-9**
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** or **uridine** source for increasing cytidine levels in vivo and treating cytidine-dependent human **neurol**. diseases)

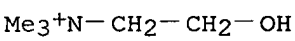
RN 54-03-5 HCAPLUS
CN Benzoic acid, 3,4,5-trimethoxy-, 1,2-ethanediylbis[(methylimino)-3,1-propanediyl] ester (9CI) (CA INDEX NAME)



RN 62-49-7 HCAPLUS
CN Ethanaminium, 2-hydroxy-N,N,N-trimethyl- (9CI) (CA INDEX NAME)



RN 67-48-1 HCAPLUS
CN Ethanaminium, 2-hydroxy-N,N,N-trimethyl-, chloride (9CI) (CA INDEX NAME)

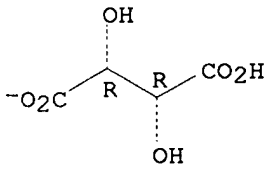


RN 87-67-2 HCAPLUS
CN Ethanaminium, 2-hydroxy-N,N,N-trimethyl-, salt with (2R,3R)-2,3-dihydroxybutanedioic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

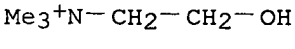
CRN 49681-69-8
CMF C4 H5 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.

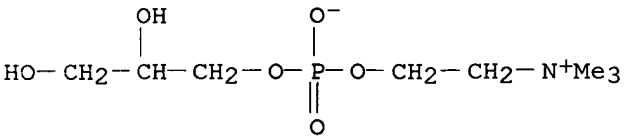


CM 2

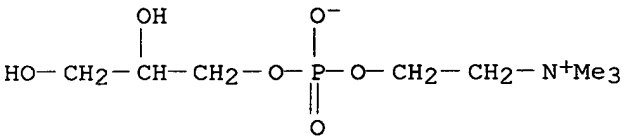
CRN 62-49-7
CMF C5 H14 N O



RN 563-24-6 HCAPLUS
CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)

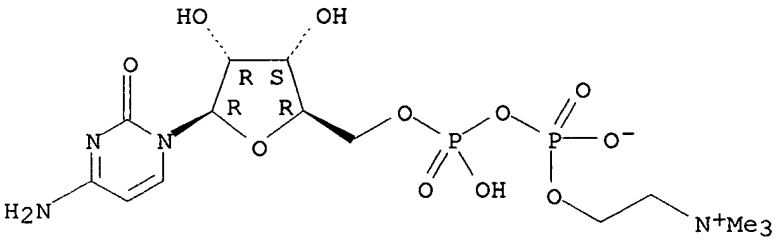


RN 563-24-6 HCAPLUS
CN Ethanaminium, 2-[[(2,3-dihydroxypropoxy)hydroxyphosphinyl]oxy]-N,N,N-trimethyl-, inner salt (9CI) (CA INDEX NAME)

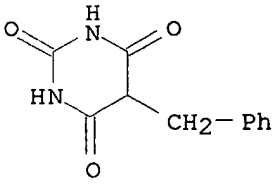


RN 987-78-0 HCAPLUS
CN Cytidine 5'-(trihydrogen diphosphate), P'-[2-(trimethylammonio)ethyl] ester, inner salt (9CI) (CA INDEX NAME)

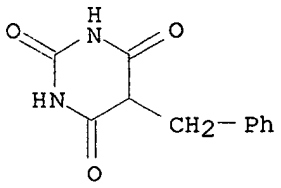
Absolute stereochemistry.



RN 5909-45-5 HCAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(phenylmethyl)- (9CI) (CA INDEX NAME)

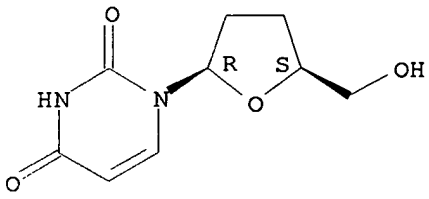


RN 5909-45-5 HCAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(phenylmethyl)- (9CI) (CA INDEX NAME)

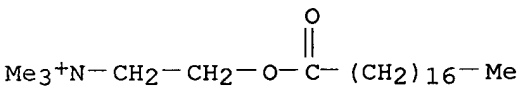


RN 5983-09-5 HCAPLUS
CN Uridine, 2',3'-dideoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

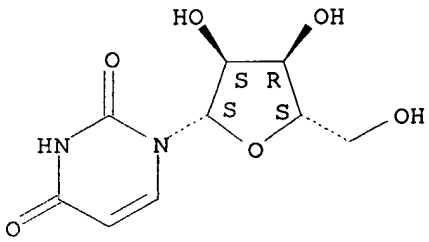


RN 23464-76-8 HCAPLUS
CN Ethanaminium, N,N,N-trimethyl-2-[(1-oxooctadecyl)oxy]- (9CI) (CA INDEX NAME)



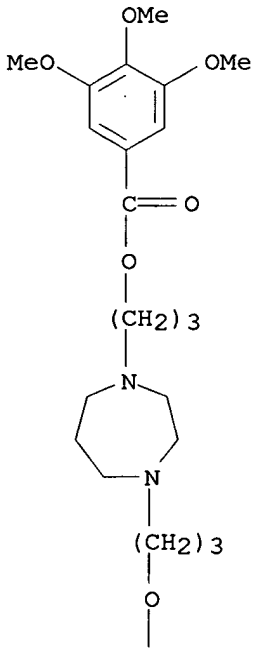
RN 26287-69-4 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-.beta.-L-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

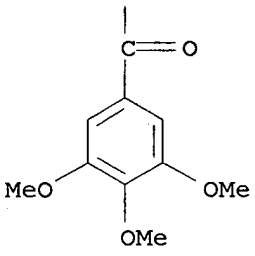


RN 35898-87-4 HCAPLUS
CN Benzoic acid, 3,4,5-trimethoxy-, (tetrahydro-1H-1,4-diazepine-1,4(5H)-diyl)di-3,1-propanediyl ester (9CI) (CA INDEX NAME)

PAGE 1-A

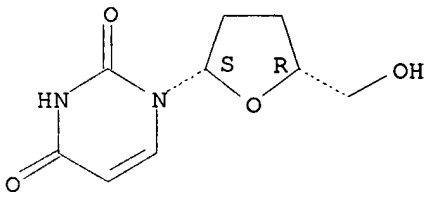


PAGE 2-A



RN 153547-98-9 HCAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[(2S,5R)-tetrahydro-5-(hydroxymethyl)-2-furanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L48 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:635462 HCAPLUS
DN 131:237984
TI **uridine** for treatment of neuron degenerative diseases
IN Piazza, Cinzia; Politi, Vincenzo; Materazzi, Mario
PA Polifarma S.p.A., Italy
SO U.S., 7 pp.

CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-55
NCL 514269000
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5962459	A	19991005	US 1997-862306	19970523
PRAI	US 1996-18543		19960529		

AB **Uridine** is a therapeutic agent active as a growth promoter for treatment of neuron degenerative diseases deriving from pathol. aging or selective destruction. In particular, **uridine** shows the same biol. effects as NGF, when added at low doses to the culture medium, so that **uridine** may replace NGF as therapeutic agent in neural diseases and it may be also assocd. with other growth factors that allow differentiation of neurons, or with antitumor and antiviral drugs that cause neuron damage. In addn. **uridine** shows important trophic properties on various types of cultured cells, stimulating cell reprodn. when used at rather high dose levels.

ST **uridine neurodegenerative** disease treatment

IT **Nervous** system
(amyotrophic lateral sclerosis; **uridine** for treatment of neuron degenerative diseases)

IT Anti-AIDS agents
(antiviral agent peripheral nervous-system-harming effect; **uridine** for treatment of neuron degenerative diseases)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**brain**-derived; **uridine** for treatment of neuron degenerative diseases)

IT Antitumor agents
(cell-harming effects; **uridine** for treatment of neuron degenerative diseases)

IT **Nervous** system
(degeneration; **uridine** for treatment of neuron degenerative diseases)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glial-derived; **uridine** for treatment of neuron degenerative diseases)

IT Antiviral agents
(peripheral nervous-system-harming effects; **uridine** for treatment of neuron degenerative diseases)

IT Nerve, disease
(peripheral neuropathy; **uridine** for treatment of neuron degenerative diseases)

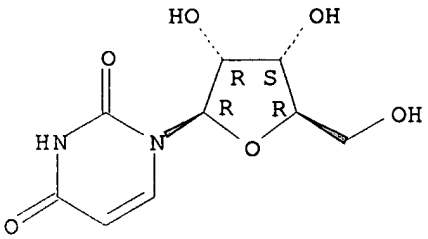
IT **Nervous** system
(peripheral; **uridine** for treatment of neuron degenerative diseases)

IT **Brain**, disease
(stroke, nervous system disturbance from; **uridine** for treatment of neuron degenerative diseases)

IT Anti-**Alzheimer**'s agents
Antiparkinsonian agents
Cell differentiation
Cell proliferation
Drug delivery systems
Drug interactions
Nervous system agents
Neuroglia
Neuron

(**uridine** for treatment of neuron degenerative diseases)
IT Ciliary neurotrophic factor
Growth factors, animal
Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** for treatment of neuron degenerative diseases)
IT Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; **uridine** for treatment of neuron degenerative diseases)
IT 7481-89-2, DdC 30516-87-1, AZT
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**uridine** for treatment of neuron degenerative diseases)
IT **58-96-8, Uridine** 9061-61-4, Nerve growth factor
62031-54-3, Fibroblast growth factor 67763-96-6, Insulin-like growth factor 1 130939-66-1, Neurotrophin 3 143375-33-1, Neurotrophin 4
148499-03-0, Neurotrophin 5
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**uridine** for treatment of neuron degenerative diseases)
RE.CNT 11
RE
(1) Agnati; Acta Physiol Scand 1986, V126(4), P525 HCAPLUS
(2) Anon; EP 0178267 1986 HCAPLUS
(3) Anon; EP 0348360 1989 HCAPLUS
(4) Anon; EP 0462075 1991 HCAPLUS
(5) Anon; JP 05304951 1993 HCAPLUS
(6) Benzi, G; Biochemical Pharmacology 1983, V32(6), P1083 HCAPLUS
(7) Engal, W; Neurology 1988, V38(3, supplement 1), P326
(8) Keilbaugh, S; Molec Pharmacology 1993, V44(4), P702 HCAPLUS
(9) Merck & Co; The Merck Index, Twelfth Edition 1996, P1113
(10) Mervis; Ann NY Acad Sci 1991, P95 HCAPLUS
(11) Wakade, T; Journal of Physiology 1995, V488(1), P123 HCAPLUS
IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**uridine** for treatment of neuron degenerative diseases)
RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:184143 HCAPLUS
DN 130:218318
TI Use of purine nucleosides for modulating the axonal outgrowth of central nervous system neurons
IN Benowitz, Larry I.
PA Children's Medical Center Corporation, USA
SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-70
ICS A61K031-52
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9911274	A1	19990311	WO 1998-US3001	19980220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866568	A1	19990322	AU 1998-66568	19980220
EP 1009412	A1	20000621	EP 1998-908565	19980220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-921902 19970902
WO 1998-US3001 19980220

AB Methods and compns. for modulating the axonal outgrowth of central nervous system neurons are provided. Methods for stimulating the axonal outgrowth of central nervous system neurons following an injury (e.g., stroke, Traumatic **Brain** Injury, **cerebral** aneurism, **spinal** cord injury and the like) and methods for inhibiting the axonal outgrowth of central nervous system neurons in conditions such as epilepsy, e.g., post-traumatic epilepsy, and neuropathic pain syndrome, are also provided. These methods generally involve contacting the central nervous system neurons with a purine nucleoside, or analog thereof. Preferably, inosine or guanosine is used to stimulate axonal outgrowth and 6-thioguanine is used to inhibit axonal outgrowth. The methods and compns. are particularly useful for modulating the axonal outgrowth of mammalian central nervous system neurons, such as mammalian retinal ganglion cells. Pharmaceutical and packaged formulations that include the purine nucleosides, and analogs thereof, of the invention are also provided.

ST purine nucleoside pharmaceutical axon outgrowth; nervous system agent purine nucleoside axon

IT Meninges
(cerebellomedullary cistern, drug administration to; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

IT Aneurysm
(**cerebral**; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

IT Liquid dosage forms (drug delivery systems)
(dispersions; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

IT **Cerebral** ventricle
Cerebrospinal fluid
Lumbar **spinal** cord
(drug administration to; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

IT Lipids, biological studies
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(formulations contg.; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

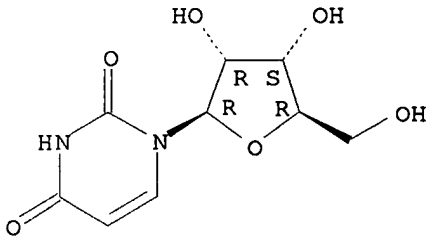
IT Infusions (drug delivery systems)
(minipumps; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

IT Pain
(neuropathic; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
IT Paralysis
(paraplegia; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
IT Epilepsy
(post-traumatic; purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
IT Analgesics
Anticonvulsants
Brain trauma
Ganglion cell (retinal)
Liposomes (drug delivery systems)
Nervous system agents
Neurite outgrowth
Spinal cord injury
Stroke
Sustained release drug delivery systems
(purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
IT Purine nucleosides
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
IT 50-89-5, Thymidine, biological studies 56-65-5, 5'-ATP, biological studies 58-61-7, Adenosine, biological studies 58-63-9, Inosine 58-64-0, 5'-ADP, biological studies **58-96-8**, **Uridine** 60-92-4, CAMP 61-19-8, Adenosine 5'-monophosphate, biological studies 65-46-3, Cytidine 68-94-0, **Hypoxanthine** 69-89-6, Xanthine 85-31-4, 6-Thioguanosine 118-00-3, Guanosine, biological studies 131-99-7, 5'-Inosine monophosphate 146-77-0, 2-Chloroadenosine 362-74-3, Dibutyryl cAMP 7665-99-8, CGMP 31356-94-2, 8-Bromo cyclic GMP 38048-32-7 51350-19-7, erythro-9-(2-Hydroxy-3-nonyl)adenine 54364-02-2 152322-58-2
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)

RE.CNT 6
RE
(1) Benowitz, L; DATABASE BIOSIS PREVIES 1997
(2) Greene, L; J NEUROSCI 1990, V10(5) HCAPLUS
(3) Gysbers, J; INT J DEV NEUROSCI 1996, V14(1) HCAPLUS
(4) Gysbers, J; NEUROREPORT 1992, V3(11), P997 HCAPLUS
(5) Medcament, P; WO 9400132 A 1994
(6) Svensson, B; EUR J NEUROSCI 1993, V5(8) MEDLINE

IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(purine nucleosides and analogs for modulating the axonal outgrowth of central nervous system neurons)
RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



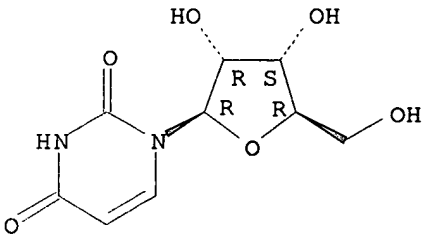
L48 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:569857 HCAPLUS
DN 129:314450
TI A syndrome of seizures and pervasive **developmental disorder** associated with excessive cellular nucleotidase activity
AU Page, Theodore; Yu, Alice; Fontenessi, John; Nyhan, William
CS Dep. Neurosciences and Dep. Pediatrics, University California, La Jolla, CA, 92093, USA
SO Adv. Exp. Med. Biol. (1998), 431(Purine and Pyrimidine Metabolism in Man IX, 1998), 789-792
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Publishing Corp.
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
AB A unique type of pervasive **developmental disorder** (PDD) is reported, which is assocd. with seizures and other neurol. symptoms, abnormal speech and behavior, and increased susceptibility to infection. All of these patients showed excessive 5'-nucleotidase in their fibroblast lysates. Metabolic therapy with oral **uridine** brought about dramatic improvement in every case.
ST **mental disorder** seizure nucleotidase **uridine**
IT **Mental disorders**
(pervasive **developmental disorder**; syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase **activity**, in humans)
IT Seizures
(syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase activity, in humans)
IT Purine nucleotides
Pyrimidine nucleotides
RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase activity, in humans)
IT 64-18-6, Formic acid, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(incorporation into pyrimidine nucleotides; syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase activity, in humans)
IT 9027-73-0, 5'-Nucleotidase
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase activity, in humans)
IT **58-96-8, Uridine**
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(syndrome of seizures and pervasive **developmental**

disorder assocd. with excessive cellular nucleotidase activity, in humans)

IT **58-96-8, Uridine**
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(syndrome of seizures and pervasive **developmental disorder** assocd. with excessive cellular nucleotidase activity, in humans)

RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:803819 HCAPLUS
DN 128:30410
TI **Uridine**-comprising therapeutic active agent for treatment of **neurodegenerative** disorders
IN Piazza, Cinzia; Politi, Vincenzo
PA Polifarma S.P.A., Italy
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-70
CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745127	A1	19971204	WO 1997-IT117	19970523
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9730468	A1	19980105	AU 1997-30468	19970523
	EP 914131	A1	19990512	EP 1997-925266	19970523
	R: AT, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT, FI				
	BR 9709379	A	20000111	BR 1997-9379	19970523
	JP 2000503668	T2	20000328	JP 1997-541970	19970523
PRAI	IT 1996-RM364		19960528		
	WO 1997-IT117		19970523		

AB **Uridine** is a therapeutic agent active as a growth promoter for treatment of neuron degenerative diseases deriving from pathol. ageing or selective destruction. In particular **uridine** shows the same biol. effects as NGF when added at low doses to the culture medium, so that **uridine** may replace NGF as therapeutic agent in neural diseases and it may be also assocd. to other growth factors that allow neuron's differentiation, or with anti-cancer and anti-virus drugs that cause neuron damage. In addn. **uridine** shows important trophic

properties on various types of cultured cells, stimulating cell reprodn. when used at rather high dose levels.

ST **neurodegenerative** disease therapeutic **uridine**

IT Peripheral neuropathy
(iatrogenic; **uridine** for treatment of **neurodegenerative** disorders)

IT **Brain**-derived neurotrophic factor
Ciliary neurotrophic factor
Glial-derived neurotrophic factor
Neurotrophic factors
Transforming growth factors .beta.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimic for; **uridine** for treatment of **neurodegenerative** disorders)

IT AIDS (disease)
(peripheral nervous system disorder from virucide against; **uridine** for treatment of **neurodegenerative** disorders)

IT Antiviral agents
(peripheral nervous system disorder from; **uridine** for treatment of **neurodegenerative** disorders)

IT Antitumor agents
(peripheral neuropathy from; **uridine** for treatment of **neurodegenerative** disorders)

IT **Alzheimer**'s disease
Amyotrophic lateral sclerosis
Cell proliferation
Differentiation inducers
Drug delivery systems
Glial cells
Nervous system agents
Neurodegenerative diseases
Neuroprotectants
Neurotoxicity
Parkinson's disease
Stroke
(**uridine** for treatment of **neurodegenerative** disorders)

IT 9061-61-4, Nerve growth factor 62031-54-3, Fibroblast growth factor 67763-96-6, Insulin-like growth factor I 130939-66-1, Neurotrophin 3 143375-33-1, Neurotrophin 4 148499-03-0, Neurotrophin 5
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimic for; **uridine** for treatment of **neurodegenerative** disorders)

IT 7481-89-2, DdC 30516-87-1, AZT
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(toxicity; **uridine** for treatment of **neurodegenerative** disorders)

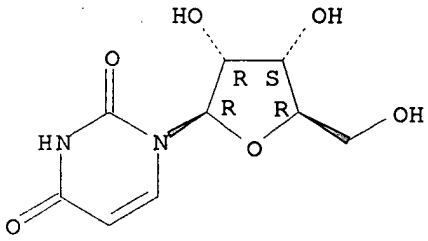
IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**uridine** for treatment of **neurodegenerative** disorders)

IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**uridine** for treatment of **neurodegenerative** disorders)

RN 58-96-8 HCAPLUS

CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:772604 HCAPLUS
DN 128:43875
TI Solution and process for resuscitation and reparation of **ischemically** damaged tissue
IN Brasile, Lauren
PA Breonics, Inc., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N001-02
ICS A61M001-00; A61M031-00
CC 1-12 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743899	A1	19971127	WO 1997-US8205	19970516 <--
	W: AU, CA, CN, JP, RU				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2255657	AA	19971127	CA 1997-2255657	19970516 <--
	AU 9730671	A1	19971209	AU 1997-30671	19970516 <--
	CN 1226132	A	19990818	CN 1997-195768	19970516 <--
	EP 1021084	A1	20000726	EP 1997-925571	19970516 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-649200 19960517 <--
WO 1997-US8205 19970516 <--

AB A process and resuscitation soln. are disclosed for inducing repair of **ischem**. damaged organs and tissues, to the degree that impairment of function can be reversed; and preventing further tissue damage during restoration of the circulation of the treated organ or tissue. The process comprises flushing the organ with the resuscitation soln. of the invention at a warm temp. of approx. 28-37.degree.C to remove accumulated blood and acidotic products from blood flow deprivation; and perfusing the flushed organ or tissue with the resuscitation soln., wherein the soln. contains a novel combination of components to provide for (i) dilating of the blood vessels within the organ or tissue, (ii) reestablishing organ or tissue function by supplying trophic factors, (iii) restoring cellular integrity and function to the **ischem**. damaged organ or tissue, and (i.v.) reestablishing oxidative metab. by readapting the **ischem**. damaged organ or tissue, surviving by anaerobic respiration, to an oxygenated resuscitation soln.

ST tissue organ **ischemia** resuscitation; soln resuscitation **ischemia** tissue organ

IT Prostaglandins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(I; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

IT Acidosis
(acidotic products; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

IT Renal transplant
(allograft; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Electron transport system (biological)
Tricarboxylic acid cycle
(components; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Nucleic acids
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs.; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Energy metabolism (animal)
(energy substrates; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Allograft
Autotransplant
(kidney; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Flow
(rate; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Respiration (animal)
Therapy
(resuscitation; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT **Anti-ischemic** agents
Antioxidants
Blood
Blood pressure
Blood vessel
Calcium channel blockers
Erythrocyte
Neuroprotectants
Oxidative metabolism
Perfusion
Pumps
Renal **ischemia**
Respiratory air
Solutions (drug delivery systems)
Vascular resistance
Vasodilators
pH
(soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Amino acids, biological studies
Hemoglobins
Nucleosides, biological studies
Perfluoro compounds
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Vascular endothelium
(substrates for endothelial cell-mediated vasodilation; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Microvessel
(substrates for microvessel vasodilation; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT Growth factors (animal)
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trophic factors; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)
IT 73-24-5D, Adenine, derivs.

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenine compd. pool components; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

IT 7782-44-7, Oxygen, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(and oxygenators and oxygen carriers; soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

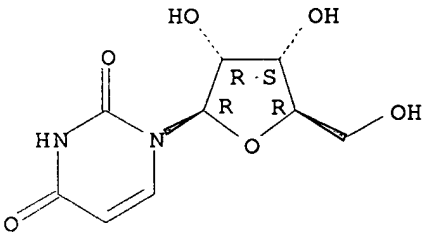
IT 50-89-5, Thymidine, biological studies 50-99-7, Glucose, biological studies 51-84-3, **Acetylcholine**, biological studies 52-53-9, Verapamil 53-84-9, NAD 56-65-5, Adenosine triphosphate, biological studies 58-61-7, Adenosine, biological studies 58-68-4, NADH **58-96-8, Uridine** 61-19-8, Adenosine monophosphate, biological studies 63-39-8, UTP 65-46-3, Cytidine 70-18-8, Glutathione, biological studies 74-79-3, L-Arginine, biological studies 85-61-0, Coenzyme A, biological studies 118-00-3, Guanosine, biological studies 127-17-3, Pyruvic acid, biological studies 146-14-5, Flavin adenine dinucleotide 154-87-0, Thiamine pyrophosphate chloride 951-77-9, Deoxycytidine 958-09-8, Deoxyadenosine 961-07-9, Deoxyguanosine 7439-95-4, Magnesium, biological studies 9004-10-8, Insulin, biological studies 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 12619-70-4, Cyclodextrin 16887-00-6, Chloride, biological studies 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

IT 124-38-9, Carbon dioxide, biological studies
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

IT **58-96-8, Uridine**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(soln. and process for resuscitation and reparation of **ischem**. damaged tissue)

RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



L48 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:672984 HCAPLUS
DN 127:344939
TI **Developmental disorder** associated with increased cellular nucleotidase activity
AU Page, Theodore; Yu, Alice; Fontanesi, John; Nyhan, William L.
CS Departments Neurosciences Pediatrics, University California San Diego, La Jolla, CA, 92093, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1997), 94(21), 11601-11606
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences
DT Journal
LA English
CC 14-14 (Mammalian Pathological Biochemistry)
AB Four unrelated patients are described with a syndrome that included developmental delay, seizures, **ataxia**, recurrent infections, severe language deficit, and an unusual behavioral phenotype characterized by hyperactivity, short attention span, and poor social interaction. These manifestations appeared within the first few years of life. Each patient displayed abnormalities on EEG. No unusual metabolites were found in plasma or urine, and metabolic testing was normal except for persistent hypouricosuria. Investigation of purine and pyrimidine metab. in cultured fibroblasts derived from these patients showed normal incorporation of purine bases into nucleotides but decreased incorporation of **uridine**. De novo synthesis of purines and cellular phosphoribosyl pyrophosphate content also were moderately decreased. The distribution of incorporated purines and pyrimidines did not reveal a pattern suggestive of a deficient enzyme activity. Assay of individual enzymes in fibroblast lysates showed no deficiencies. However, the activity of cytosolic 5'-nucleotidase was elevated 6- to 10-fold. Based on the possibility that the obsd. increased catabolic activity and decreased pyrimidine salvage might be causing a deficiency of pyrimidine nucleotides, the patients were treated with oral pyrimidine nucleoside or nucleotide compds. All patients showed remarkable improvement in speech and behavior as well as decreased seizure activity and frequency of infections. A double-blind placebo trial was undertaken to ascertain the efficacy of this supplementation regimen. Upon replacement of the supplements with placebo, all patients showed rapid regression to their pretreatment states. These observations suggest that increased nucleotide catabolism is related to the symptoms of these patients, and that the effects of this increased catabolism are reversed by administration of **uridine**.
ST nucleotidase **development disorder**
IT **Ataxia**
Behavior (animal)
Brain electric activity
Seizures
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT Pyrimidine nucleotides
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT **Development** (mammalian postnatal)
(**disorder; developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT 9027-73-0, 5'-Nucleotidase
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT 7540-64-9, Phosphoribosyl pyrophosphate
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT **58-96-8, Uridine**
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
IT **58-96-8, Uridine**
RL: BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(**developmental disorder** assocd. with increased cellular nucleotidase activity in humans)
RN 58-96-8 HCAPLUS
CN Uridine (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.